Hospitalisation and length of hospital stay following first-episode psychosis: systematic review and meta-analysis of longitudinal studies

Subtitle: Meta-analysis of service-use outcomes in psychosis

Olesya Ajnakina*[1, 2], Brendon Stubbs [3, 4], Emma Francis [3], Fiona Gaughran [5, 6], Anthony S. David [7], Robin M. Murray [5, 8], John Lally [5, 9, 10]

[1] Department of Biostatistics & Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, University of London, London, United Kingdom

[2] Department of Behavioural Science and Health, Institute of Epidemiology and Health Care, University College London, London, United Kingdom

[3] Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom

[4] Physiotherapy Department, South London and Maudsley NHS Foundation Trust, London, United Kingdom

[5] Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom

[6] National Psychosis Service, South London and Maudsley NHS Foundation Trust, London, United Kingdom

[7] Institute of Mental Health, University College London, London, United Kingdom

[8] Department of Psychiatry, Experimental Biomedicine and Clinical Neuroscience (BIONEC), University of Palermo, Italy

[9] Department of Psychiatry, Royal College of Surgeons in Ireland, Dublin, Ireland

[10] Department of Psychiatry, School of Medicine and Medical Sciences, University College Dublin, St Vincent's University Hospital, Dublin, Ireland

***Address for correspondence:** Dr Olesya Ajnakina, Department of Biostatistics & Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, University of London, 16 De Crespigny Park, Denmark Hill, London SE5 8AF; Email: olesya.ajnakina@kcl.ac.uk

FUNDED BY
NIHR | National Institute for Health Research

Abstract

Background: Reducing hospitalisation and length of stay (LOS) in hospital following first episode psychosis (FEP) is important, yet reliable measures of these outcomes and their moderators are lacking. We conducted a systematic review and meta-analysis to investigate the proportion of FEP cases who were hospitalised after their first contact with services and the LOS in hospital during follow-up.

Methods: Studies were identified from a systematic search across major electronic databases from inception to October 2017. Random effects meta-analyses and meta-regression analyses were conducted.

Results: 81 longitudinal studies encompassing data for 23280 FEP patients with an average follow-up length of 7 years were included. 55% (95%CI=50.3-60.5%) of FEP cases were hospitalised at least once during follow-up with the pooled average LOS of 116.7 days (95%CI=95.1-138.3). Older age of illness onset and being in a stable relationship were associated with a lower proportion of people who were hospitalised. While the proportion of hospitalised patients has not decreased over time, LOS has, with the sharpest reduction in the latest time period. The proportion of patients hospitalised during follow-up was highest in Australia and New Zealand (78.4%) compared to Europe (58.1%) and North America (48.0%); and lowest in Asia (32.5%). Black ethnicity and longer duration of untreated psychosis were associated with longer LOS; while less severe psychotic symptoms at baseline were associated with shorter LOS.

Conclusion: One in two FEP cases required hospitalisation at least once during a 7-year follow-up with an average length of hospitalisation of 4 months during this period. LOS has declined over time, particularly in those countries in which it was previously longest.

Key words: First episode psychosis / schizophrenia / hospitalisation / length of stay / inpatient / follow-up / outcome

Introduction

Psychotic disorders are a major cause of morbidity and premature mortality affecting approximately 3% of the general population (van Os *et al*., 2009). They are associated with a significant public health burden worldwide (Knapp *et al*., 2004) with approximately half of the costs attributable to hospitalisation (Kennedy *et al*., 2014; Sledge *et a*l., 1996).

Even though hospitalisation for psychosis has been a common outcome measure in longitudinal studies for the past 40 years, it remains unclear how many patients require hospital admission in the years after FEP. Some studies have reported that 30% or fewer patients with FEP are hospitalised at least once during their illness course (Salem *et al*., 2009; Stirling *et al*., 2003; Ucok *et al*., 2006) while others found that as many as 90% required hospital care after their first contact with mental health services (Berge *et al*., 1983; Lehtinen *et al*., 2000). Similarly, wide variations in the length of stay (LOS) in psychiatric inpatient units have been reported with average durations ranging from 20 days to 740 days (Fraguas *et al*., 2014; Turner *et al*., 2009). Methodological variations accounting for some of this heterogeneity preclude the development of a reliable picture of hospital use in patients after FEP (Eaton *et al*., 1992). There is also the question of the generalisability of studies as a large proportion were conducted in high-income counties (Patel *et al*., 2007; Saxena *et al*., 2006). Thus, the current depiction of illness course is driven by findings obtained in the countries that are known for superior health-care rather than being globally representative.

It is important to provide unbiased and generalisable estimates of how many FEP cases will require hospitalisation after their first contact with services and of the time they will spend in inpatient care during their illness course. This will contribute to a better understanding of treatment needs for these individuals and aid service development and planning (Friis *et al*., 2016). It is equally important to identify moderating factors for these outcomes which may help to identify those FEP cases who may be at greater risk of poor long-term outcomes (Friis *et al*., 2016; Lally & Gaughran, 2018). However, no previous study has conducted a meta-

analysis incorporating global data and considered the moderators of hospital admission and LOS with meta-regression, which may identify important variables that influence these outcomes.

Therefore, the aims of the study were to conduct a systematic review and meta-analysis of all longitudinal studies that investigated the proportion of people with FEP who were hospitalised at least once during follow-up and/or reported average LOS during this period; and further to identify the moderators for these outcomes. Given the drive to reduce LOS and hospital admission, we hypothesised that the number of patients who required inpatient care, and the average LOS during follow-up would be significantly lower in the studies conducted in the last 20 years compared to earlier studies.

Methods

This systematic review was conducted and reported according to the Meta-analysis of Observational Studies in Epidemiology guidelines (Stroup *et al*., 2000) and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) (Moher *et al*., 2009).

Search Strategy

Two independent authors (JL, OA) searched PubMed, Medline, and Scopus without language restrictions from database inception to 1st October 2017. Key words used were ("first episode psychosis" OR "early episode psychosis" OR "FEP" OR "schizophrenia" OR "schiz*") AND ("admission" OR "hospitalisation" OR "hospitalization" OR "hospital*" AND "outcome" OR "follow-up"). A manual search of the reference lists of the retrieved articles was conducted.

Articles were initially screened based on title and abstract. The full texts of potentially eligible articles were independently inspected by two of the authors (O.A., J.L.). When data

were incomplete, the corresponding author was contacted and invited to send additional information. When studies reported on overlapping samples, details of the study with the longest follow-up were included. If this was unclear, studies with the largest study sample for each respective outcome were included. We included multi-site studies and retained data for the entire cohort and not for individual sites.

Inclusion and exclusion criteria

We included longitudinal studies, incorporating both retrospective and prospective study designs, which were conducted in patients with FEP (including first episode schizophrenia and first episode affective psychosis) irrespective of clinical setting (i.e., inpatient, outpatient or mixed) that fulfilled the following criteria: 1) studies reporting the a) proportion of patients who were hospitalised at least once during the follow-up period; and b) average LOS in psychiatric hospitals during the entire follow-up period; 2) studies including individuals with FEP who were making their first contact with mental health services for psychosis; 3) studies using a specified standardised diagnostic system (e.g., International Classification of Diseases (ICD versions 8, 9 and 10), Diagnostic and Statistical Manual of Mental Disorders (DSM versions III and IV), and the Research Diagnostic Criteria (RDC); 4) studies with a follow-up period ≥12 months; and 5) English language articles published in peer-reviewed journals.

We excluded studies if they: 1) were Randomised Control Trials, due to the potential that any structured intervention beyond routine care could influence the primary outcomes outlined in this meta-analysis; 2) assessed the feasibility and effectiveness of different treatment strategies for psychotic disorders; 3) were of organic psychosis due to medical conditions (i.e psychosis secondary to medical condition, such as encephalitis or epilepsy) or non-FEP cohorts; and 4) did not report quantitative data;

Data Extraction

Three authors (J.L., O.A., E.F.) extracted all data using a predetermined data extraction form and any inconsistencies were resolved by consensus. The data extracted included first author, study participant details, including mean age (years) at illness onset and first contact with mental health services, gender, country, setting (i.e., inpatient, outpatients (community), mixed, in- and out-patient settings), population, study design (i.e., prospective, retrospective), diagnostic classification method, assessment type, economic income status of the countries, duration of untreated psychosis (DUP), socio-demographic characteristics of the sample at the time of recruitment (i.e., proportion of patients who were employed, single or in a stable relationship at the study entry), baseline psychotic symptoms (mean scores), length of study follow-up, attrition, proportion hospitalised and average LOS, the proportion of patients who were taking antipsychotic medications at the study entry and at the end of follow-up, compliance with antipsychotic medications during the follow-up period, and socio-demographic characteristics at the end of follow-up (i.e., proportion of patients who were employed, single or in a stable relationship at the end of the follow-up period). A more detailed definition of these variables is provided in Supplementary Materials.

Definitions of outcomes

The co-primary outcomes were:

1. the proportion of people with FEP who were hospitalised at least once during the follow-up period (excluding any hospitalisation which occurred during the first contact for FEP)
2. the average LOS in psychiatric hospitals defined as the average (mean and the standard deviation measured in days) time spent in hospital during the follow-up period excluding any hospitalisation which occurred during the first contact for FEP.

Statistical analysis

All analysis was conducted with Comprehensive Meta-Analysis software (CMA, Version 3) and RStudio version 3.4.4 (Integrated Development for R. RStudio, Inc., Boston). The pooled prevalence of hospitalisation and average LOS was calculated using a random-effects model (Borenstein *et al*., 2010). The random-effects model was chosen to account for the influence of the context of care on these outcomes. To examine potential effects of specific factors on the primary outcomes, we further stratified these analyses according to: 1) baseline diagnosis, 2) assessment types; 3) length of follow-up; 4) study region; 5) study settings, and 6) economic income status of the country in which the study was conducted. The summary statistics were illustrated with a forest plot and funnel plot (Duval *et al*., 2000; Phan *et al*., 2014).

To investigate the variables that may influence the outcomes we conducted an unrestricted maximum likelihood meta-regression. The included moderating factors were age at illness onset, age at first contact with mental health services, male gender, ethnicity, baseline psychotic symptoms (mean scores), relationship and employment status at baseline, DUP, duration of follow-up, attrition rate, study year, treatment with antipsychotic medications at baseline and during follow-up, and compliance with antipsychotic medications during the entire follow-up period.

Publication bias was assessed with the funnel plot, Egger regression test (Opjordsmoen *et al*., 2010). We also adjusted for the presence of any publication bias calculating the Duval and Tweedie “trim-and-fill” method (Tohen *et al*., 1992). Heterogeneity was measured with the Q statistic yielding a chi-square and *p*-value, and the I^2 statistic with scores above 50% and 75% indicating moderate and high heterogeneity, respectively (Higgins *et al*., 2003). Statistical significance was considered to be at or below the 0.05 level.

Results

Search results and included participants

The flowchart of the article selection process is depicted in **Figure 1** and descriptive characteristics of each study are outlined in Supplementary Table 1. The search yielded 1434 non-duplicated publications, which were considered at the title and abstract level; 382 of these were extracted for full text review, of which 81 met the inclusion criteria with a total sample of 23280 FEP patients (range=20-12071). The mean age at illness onset in these studies was 23.5 years (SD=5.7), while mean age at first contact with mental health services was 27.3 year (SD=64); 42.3% were female and 59.3% had a baseline diagnosis of first episode schizophrenia.

Meta-analysis of hospitalisation

The proportion of people with FEP who were hospitalised at least once during the follow-up, together with heterogeneity and trim-and-fill analyses, is presented in **Table 1**. In total, 60 studies reported on the number of people with FEP who were hospitalised at least once during the follow-up period. Average length of follow-up across these studies was 7.6 years (SD=6.1, interquartile range (IQR)=2-11.8). The total sample at the end of the follow-up period was 19675 FEP cases (range=20-12071, IQR=47-149). The pooled proportion of hospitalised FEP patients during follow-up was 55.4% (95%CI=50.3-60.5, Q=3575.1, I^2=98.5). The Begg-Mazumdar (Kendall's tau b=-0.005, P=0.957) and Egger test (t=-2.53, df=56, p=0.014) indicated no publication bias.

Subgroup analyses of hospitalisation

Stratified proportions of FEP patients who were hospitalised at least once during the follow-up period, together with heterogeneity and trim-and-fill analyses are presented in **Table 1**. The proportion of patients hospitalized during follow-up was significantly higher in studies from Australia and New Zealand (78.4%, 95%CI=59.2-97.5, I^2=98.4, *Q*=203.7) compared to studies from Europe (58.1%, 95%CI=50.7-65.5, I^2=97.1, *Q*=1212.1) and North America (48.0%, 95%CI=34.5-61.6, I^2=95.4, *Q*=213.6); the lowest proportion of hospitalised patients was reported in studies from Asia (32.5%, 95%CI=25.3-41.4, I^2=81.4, *Q*=39.7). The pooled proportion of hospitalised patients during follow-up was highest in studies which were conducted in high-income countries (57.9%, 95%CI=51.7-64.1, I^2=98.4, *Q*=2833.6) compared with studies conducted in middle-income countries (34.8%, 95%CI=20.0-49.6, I^2=96.0, *Q*=355.8). The trim-and-fill method demonstrated that the proportion of patients who required hospitalisation at least once during the follow-up period in the middle-income countries was 42.9% (95%CI=27.4-56.5) when adjusted for potentially missing studies. There were no studies from low-income countries.

Effect of moderator variables influencing hospitalisation

Full details of the moderators of hospitalisation during the follow-up period are presented in **Table 2**. A lower proportion of hospitalised patients during follow-up was associated with an older age of illness onset (β=-0.049, 95%CI=-0.092 - -0.005, p=0.028, R^2=0.07) and having a stable relationship at baseline (β=-0.011, 95%CI= -0.018 - -0.004, p=0.004, R^2=0.33). There was a trend association between Black ethnicity and increased hospitalisation (β=0.004, 95%CI=0.000-0.009, p=0.075, R^2=0.13), and between higher loss to attrition and reduced hospitalisation during follow-up (β=-0.003, 95%CI=-0.007-0.000, p=0.080, R^2=0.04).

Meta-analysis of LOS

Average LOS across the follow-up period with heterogeneity and trim-and-fill analyses is provided in **Table 3**. In total, 37 studies reported on LOS over the follow-up period. The average LOS was 176.8 days (SD=186.7, median=106 days, IQR=76-204 days). Average length of follow-up across these studies was 7 years (mean=6.6 years, SD=6.4, IQR 2-8) with a cumulative sample of 4877 FEP cases (range=20-720, IQR=43.5-191.5). The pooled average LOS across the entire follow-up period was 116.7 days (95%CI=95.1-138.3, I^2=99.5, *Q*=4435.1). The Begg-Mazumdar (Kendall's tau b=0.18, p=0.215) and Egger test (t=4.31, df=24, p<0.001) indicated no publication bias.

Subgroup analyses of LOS

Stratified LOS during the follow-up period with heterogeneity and trim-and-fill analyses is provided in **Table 3**. The LOS was the longest in studies published from 1966-1995 (192.3 days, 95%CI=129.7-254.8, I^2=89.2, *Q*=37.1). The trim-and-fill method demonstrated that the average LOS in these studies was 216.8 days (95%CI=126.3-307.3) when adjusted for missing studies. The mean LOS appeared to decrease in more recent studies from 1996-2002 (129.9 days, 95%CI=78.8-180.9, I^2=98.9, *Q*=368.1) and 2003-2009 (97.7 days, 95%CI=55.3-139.9, I^2=99.8, *Q*=3041.4). The shortest average LOS was recorded in studies from 2010-2017 (96.6 days, 95%CI=54.0-139.2, I^2=99.3, *Q*=852.8).

Effect of moderator variables influencing LOS

Information on the moderators of LOS is presented in **Table 4**. The meta-regression analyses showed that a longer LOS was associated with Black ethnicity (β=2.905, 95%CI=1.273-4.537, p<0.001, R^2=0.14%) and longer DUP ($median_{days}$) (β=0.303, 95%CI=0.266-0.340, p<0.001, R^2=0.11). Another significant moderator of a longer mean LOS was a longer length of follow-up (β=11.707, 95%CI=6.577-16.838, p<0.001, R^2=0.21). Several

baseline factors associated with shorter average LOS were identified. A shorter average LOS was associated with White ethnicity (β=-0.181, 95%CI=-0.219- -0.143, p<0.001, R^2=0.12), reduced severity of psychotic symptoms at baseline (β=-0.019, 95%CI=-0.036- -0.003, p=0.018, R^2=0.08) and studies conducted in more recent years (β=-4.413, 95%CI=-7.456- -1.370, p=0.004, R^2=0.15).

Discussion

To our knowledge this is the first systematic review and meta-analysis to investigate the proportion of FEP cases who required hospitalisation at least once after their first contact with mental health services and the average LOS in hospital during follow-up. We found that more than half (55%) of all FEP patients required a hospitalisation over an average follow-up of 7 years after FEP. This proportion may seem high, but is not surprising considering that only 38% of FEP patients recover during follow-up (Lally *et al*., 2017), with 34% of FES patients meeting criteria for treatment resistance over a five year period (Lally *et al*., 2016).

Hospitalisation and average LOS in FEP patients

While bed capacity in psychiatric services has decreased in many developed countries since the 1950s (Raftery, 1992) supported by intensive attempts to integrate and care for people in the community (Munk-jorgensen, 1999), our findings demonstrate that the proportion of people with FEP who were admitted to hospital after their first contact with mental health services has remained stable over time. Nonetheless, in accordance with previous research (Agius *et l*., 2010; Hobbs *et al*., 2000; Leff and Trieman, 2000) we found that the average LOS in hospital for people FEP has decreased considerably over the past 20 years with the sharpest reduction observed in the last 7 years. This pattern was particularly pronounced in Australia and New Zealand. Our findings may indicate that while early intervention services

for psychosis are successful in facilitating earlier discharge from hospital (Agius *et al*., 2010); the sustained high proportion who require inpatient care over the illness course questions whether they are able to reduce the need for hospital admissions. Recent observational data indicate the benefits of antipsychotic long-acting injections and clozapine in reducing the need for hospitalisation in psychotic disorders (Tiihonen *et al*., 2017). Although we did not investigate the impact of antipsychotic long-acting injections and clozapine in reducing the need for hospitalisation in psychotic disorders in the present study, their wider use may be one route to reducing the sustained rates of hospitalisation identified in our study.

We found that the number of cases who were hospitalised at least once during follow-up did not differ significantly depending on the length of follow-up. Hospitalisation is considered an indicator of poor outcome in FEP (Lieberman *et al*., 1998; Schoeler *et al*., 2017) because it is costly and occurs when the illness becomes severe enough to warrant such an intervention (Pottick *et al.*, 2000). Accordingly, it may be argued that the longitudinal illness trajectory of psychosis is not characterised by a deteriorating course for most patients (Zipursky and Agid, 2015) as previously thought (Ropcke and Eggers, 2005; Schmidt *et al*., 1995). This is consistent with what was observed in relation to longitudinal recovery rates in patients with FEP where no evidence for worsening recovery rates with longer duration of follow up were found (Lally *et al*., 2017).

We found that the proportion of patients hospitalised during follow-up was considerably higher in high-income compared to the middle-income countries. Although this might imply a more debilitating illness course in well-developed countries (Lin and Kleinman, 1988), it could also be explained by differences in social support and family support structures and quality of mental health-care in middle-income countries where the burden of care and treatment costs tend to fall on families rather than hospitals (Patel *et al*., 2007; Saxena *et al*., 2005).

Impact of moderator variables on hospitalisation and LOS in FEP patients

The reasons for hospitalisation are complex (Schoeler *et al*., 2017) and likely to be explained by a range of clinical and social factors. Medication adherence was shown to be an important determinant for hospitalisation in patients with FEP during an 18 month follow-up study (Sfercu *et al*., 2017). However, this finding is not supported by studies with a longer follow-up period (Friis *et al.,* 2016) including the present work. Comparable to previous reports (Immonen *et al*., 2017; Ingrid *et al*., 2000; Uggerby *et al*., 2011), which identified an association between a younger age of illness onset and increased hospitalisation, we found that an older age of illness onset was associated with reduced hospitalisation, though it was not a significant moderator for LOS. Consistent with previous literature highlighting associations between DUP and poorer outcomes in patients with psychosis (Harrigan *et al*., 2003; Schimmelmann *et al*., 2008), we found that longer DUP was significantly associated with longer LOS. It has been shown that the mode of onset of first psychotic symptoms is one of the strongest predictors of the duration of DUP (Compton *et al.,* 2008), with an insidious onset of psychotic symptoms associated with a longer DUP (Ajnakina *et al.,* 2017). The type of clinical or non-clinical service with whom the first contact is made following onset of psychosis has been shown to be another important factor in determining the length of DUP (Bechard-Evans *et al.,* 2007; Ghali *et al*., 2013; Tanskanen *et al*., 2011). Thus, multiple clinical and service level factors, as well as social factors, are related to DUP, these need to be examined in more detail to ascertain the best ways to reduce the length of DUP, and potentially LOS.

In the present study Black ethnicity appeared to be an important factor influencing hospitalisation and was associated with longer inpatient care during follow-up. Black ethnicity has consistently been highlighted as a risk factor for psychosis onset (Lally *et al*., 2016; Radua *et al*., 2018), and has been associated with the development of a treatment resistant course of illness (Lally *et al*., 2016). Evidence is emerging from the UK that the longitudinal trajectory of psychosis in patients of Black ethnicity is characterised by more extensive utilisation of psychiatric services compared with patients of White British ethnicity (Ajnakina *et al*., 2017; Morgan *et al*., 2014), results supported by the present study. Considering that patients of Black

ethnicity are also at risk of becoming increasingly socially disadvantaged as their illness progresses (Ajnakina *et al*., 2017; Morgan *et al*., 2014), the need for hospitalisation and prolonged inpatient stays in those of Black ethnicity observed in the present study may be related to social adversity.

We found that being in a stable relationship at the time of first contact with FEP was associated with a reduced proportion of hospitalisation during follow-up. Being in a stable relationship may constitute improved social integration and strong social networks that have been shown to be associated with improved outcomes in FEP (Erickson *et al*., 1989). However, as it is common for individuals with psychosis to struggle to develop or maintain stable relationships (Sundermann *et al*., 2014), the protective effect of this factor may only be available to a minority of patients. Alternatively, being in a stable relationship may be indicative of a preserved premorbid level of functioning, improved outcomes and reduced hospitalisations during follow-up.

Methodological considerations

This is the first meta-analysis to investigate the proportion of FEP patients who required hospitalisation at least once after their first contact with mental health services and the average LOS in hospital during the entire follow-up period. We examined the proportion of hospitalised patients and average LOS during follow-up separately for baseline diagnosis of FEP, first episode schizophrenia and first episode affective disorders. Stratification by diagnosis allowed us to capture the most representative trajectory of illness for these diagnostic categories. Focusing on the incident sample of patients with a first presentation to services for psychosis ensured that the findings are not biased by chronicity of illness.

Notwithstanding the strengths, there are several limitations to the data and meta-analysis that warrant discussion. While we identified studies from five regions of the world, there was marked variability in the number of studies from each region, with the majority

conducted in Europe. We were unable to eliminate confounding variables relating to group differences in FEP cases that were enrolled in the different regions, and other service level confounds which may have existed between regions. This may include the variability in criteria employed that would warrant hospitalisation or prolonged hospital stays, bed availability, accessibility of community mental health services, treatment received in the community and in hospital, availability of community social supports, local mental health laws relating to involuntary hospital admission or other legal frameworks. Evidence suggests that all of these factors tend to vary between countries and regions (Burti, 2001; Saxena *et al*., 2006; Tulloch *et al*., 2012) and as such may have influenced hospitalisation and LOS across populations and studies included in the present meta-analysis. This should be taken into consideration when interpreting the study findings. Although it may be argued that studies utilising data from case notes may not have provided a reliable depiction of the clinical course of psychosis (Eaton *et al*., 1992), in the present study we found that hospitalisation and average LOS did not significantly differ depending on sources of data ascertainment. In relation to the meta-regression analyses, some of the variables might have failed to achieve statistical significance because of a lack of power due to small sample sizes. Further, we did not obtain data on important confounders such as types of treatments received or services available, lifestyle factors such as substance use, and symptom profile over the course of follow-up precluding the meta-analytic assessment of these factors as moderating and/or mediating variables. By excluding hospitalisations that occurred at the first contact with mental health services for FEP we may have omitted a small proportion of severely ill patients who might have remained hospitalised for most of the follow-up period. Finally, we were unable to establish the reasons for hospitalisation, whether it was the result of psychotic relapse, antipsychotic intolerance or a comorbid mental disorder.

Conclusion

This meta-analysis indicates that one in two patients with FEP will require hospitalisation at least once during a 7-year follow-up with an average inpatient stay of 4 months during this period. While the proportion of those with FEP who were admitted to hospital in the years following FEP has remained stable over the years, the average time FEP cases spent in hospital during follow-up has decreased in the last 20 years. This suggests that patients are now discharged earlier compared to previous time periods. While most patients and clinicians may favour shorter LOS in hospital, the question as to whether patients are discharged prematurely needs further investigation.

Financial Support

This paper represents independent research funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research (NIHR) or the Department of Health and Social Care. O.A. is funded by the National Institute for Health Research (NIHR) (NIHR Post Doctoral Fellowship - PDF-2018-11-ST2-020) for this project. R.M.M. and A.S.D. receive salary support from the NIHR Maudsley BRC. The views expressed are those of the author(s) and not necessarily those of the National Health Service (NHS), the NIHR, or the Department of Health and Social Care. FG and BS are part funded by the National Institute for Health Research Collaboration for Leadership in Applied Health Research & Care Funding scheme with support from the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care. FG also receives support from the Stanley Medical Research Institute).

Declaration of Interest

R.M.M. has received honoraria from Janssen, Astra-Zeneca, Lilly, and BMS. A.S.D. has received honoraria from Janssen and Roche Pharmaceuticals. F.G. has received honoraria for advisory work and lectures from Roche, BMS, Lundbeck, Otsuka and Sunovion and has a family member with professional links to Lilly and GSK. The other authors (O.A., B.S., J.L., E.F.) have no conflict of interest to declare.

References

Agius M, Hadjinicolaou AV, Ramkisson R, Shah S, Haq SU, Tomenson B, Zaman R. (2010). Does early intervention for psychosis work? An analysis of outcomes of early intervention in psychosis based on the critical period hypothesis, measured by number of admissions and bed days used over a period of six years, the first three in an early intervention service, the second three in a community mental health team. *Psychiatria Danubina* **22**, s72-84.

Ajnakina O, Lally J, Di Forti M, Kolliakou A, Gardner-Sood P, Lopez-Morinigo J, Dazzan P, Pariante CM, Mondelli V, MacCabe J, David AS, Gaughran F, Murray RM, Vassos E (2017) Patterns of illness and care over the 5 years following onset of psychosis in different ethnic groups; the gap-5 study. *Social Psychiatry and Psychiatric Epidemiology* **52**, 1101-11.

Ajnakina O, Morgan C, Gayer-Anderson C, Oduola S, Bourque F, Bramley S, Williamson J, MacCabe J, Dazzan P, Murray R, David A (2017). Only a small proportion of patients with first episode psychosis come via prodromal services: a retrospective survey of a large UK mental health programme. *BMC Psychiatry* **17**, 308

Bechard-Evans L, Schmitz N, Abadi S, Joober R, King S, Malla A (2007). Determinants of help-seeking and system related components of delay in the treatment of first-episode psychosis. *Schizophrenia Research* **96**, 206-14.

Berg E, Lindelius R, Petterson U, Salum I (1983). Schizoaffective psychoses. A long-term follow-up. *Acta Psychiatrica Scandinavica* **67**, 389-98.

Borenstein M, Hedges Lv, Higgins Jp, Rothstein HR (2010). A basic introduction to fixed-effect and random-effects models for meta-analysis. *Research Synthesis Methods* **1**, 97-111.

Burti L (2001). Italian psychiatric reform 20 plus years after. *Acta Psychiatrica Scandinavica* **410**, 41-6.

Compton MT, Chien V H, Leiner AS, Goulding SM, Weiss PS (2008). Mode of onset of psychosis and family involvement in help-seeking as determinants of duration of untreated psychosis. *Social Psychiatry and Psychiatric Epidemiology* **43**, 975-82.

Duval S, Tweedie R (2000). Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* **56**, 455-63.

Eaton WW, Mortensen PB, Herrman H, Freeman H, Bilker W, Burgess P, Wooff K (1992). Long-term course of hospitalization for schizophrenia: Part I. Risk for rehospitalization. *Schizophrenia Bulletin* **18**, 217-28.

Erickson DH, Beiser M, Iacono WG, Fleming JA, Lin TY (1989). The role of social relationships in the course of first-episode schizophrenia and affective psychosis. *American Journal of Psychiatry* **146**, 1456-61.

Fraguas D, Del Rey-Mejías A, Moreno C, Castro-Fornieles J, Graell M, Otero S, Gonzalez-Pinto A, Moreno D, Baeza I, Martínez-Cengotitabengoa M, Arango C, Parellada M (2014). Duration of untreated psychosis predicts functional and clinical outcome in children and adolescents with first-episode psychosis: a 2-year longitudinal study. *Schizophrenia Research* **152**, 130-8.

Friis S, Melle I, Johannessen JO, Røssberg JI, Barder HE, Evensen JH, Haahr U, Ten Velden Hegelstad W, Joa I, Langeveld J, Larsen TK, Opjordsmoen S, Rund BR,

Simonsen E, Vaglum PW1, McGlashan TH (2016). Early predictors of ten-year course in first-episode psychosis. *Psychiatric Services* **67**, 438-43.

Ghali S, Fisher HL, Joyce J, Major B, Hobbs L, Soni S, Chisholm B, Rahaman N, Papada P, Lawrence J, Bloy S, Marlowe K, Aitchison KJ, Power P, Johnson S. (2013). Ethnic variations in pathways into early intervention services for psychosis. *British Journal of Psychiatry* **202**, 277-83.

Harrigan SM, Mcgorry PD, Krstev H (2003). Does treatment delay in first-episode psychosis really matter? *Psychological Medicine* **33**, 97-110.

Harrigan SM, McGorry PD, Krstev H (2003). Does treatment delay in first-episode psychosis really matter? *Psychological Medicien* **33**, 97-110.

Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003). Measuring inconsistency in meta-analyses. *BMJ* **327**, 557-60.

Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003). Measuring inconsistency in meta-analyses. *BMJ* **327**, 557-560

Hobbs C, Tennant C, Rosen A, Newton L, Lapsley HM, Tribe K, Brown JE (2000). Deinstitutionalisation for long-term mental illness: a 2-year clinical evaluation. *Australian and New Zealand Journal of Psychiatry* **34**, 476-83.

Immonen J, Jaaskelainen E, Korpela H, Miettunen J (2017). Age at onset and the outcomes of schizophrenia: a systematic review and meta-analysis. *Early Intervention Psychiatry* **11**, 453-60.

Kennedy JL, Altar Ca, Taylor DL, Degtiar I, Hornberger JC (2014). The social and economic burden of treatment-resistant schizophrenia: a systematic literature review. *International Clinical Psychopharmacology* **29**, 63-76.

Knapp M, Mangalore R, Simon J (2004). The global costs of schizophrenia. *Schizophrenia Bulletin* **30**, 279-93.

Lally J, Ajnakina O, Di Forti M, Trotta A, Demjaha A, Kolliakou A, Mondelli V, Reis Marques T, Pariante C, Dazzan P, Shergil SS, Howes OD, David AS, MacCabe JH, Gaughran F, Murray RM (2016). Two distinct patterns of treatment resistance: clinical predictors of treatment resistance in first-episode schizophrenia spectrum psychoses. *Psychological Medicine* **8**, 1-10.

Lally J, Ajnakina O, Stubbs B, Cullinane M, Murphy KC, Gaughran F, Murray RM (2017). Remission and recovery from first-episode psychosis in adults: systematic review and meta-analysis of long-term outcome studies. British Journal of Psychiatry **211**, 350-8.

Lally J, Gaughran F (2018). Treatment resistant schizophrenia - review and a call to action. *Irish Journal of Psychological Medicine* **27**, 1-13.

Lay B, Blanz B, Hartmann M, Schmidt MH (2000). The psychosocial outcome of adolescent-onset schizophrenia: a 12-year followup. *Schizophrenia Bulletin* **26**, 801-16.

Leff J, trieman N (2000). Long-stay patients discharged from psychiatric hospitals. Social and clinical outcomes after five years in the community. The TAPS Project 46. *British Journal of Psychiatry* **176**, 217-23.

Lehtinen V, Aaltonen J, Koffert T, Rakkolainen V, Syvalahti E (2000). Two-year outcome in first-episode psychosis treated according to an integrated model. Is immediate neuroleptisation always needed? *European Psychiatry* **15**, 312-20.

Lieberman PB, Wiitala SA, Elliott B, Mccormick S, Goyette SB (1998). Decreasing length of stay: are there effects on outcomes of psychiatric hospitalization? *American Journal of Psychiatry* **155**, 905-9.

Lin KM, Kleinman AM (1988). Psychopathology and clinical course of schizophrenia: a cross-cultural perspective. *Schizophrenia Bulletin* **14**, 555-67.

Melle I, Friis S, Hauff E, Vaglum P (2005). Patients with schizophrenia after the acute ward: seven years' service utilization and clinical course. *Nordic Journal of Psychiatry* **54**, 47-54.

Moher D, Liberati A, Tetzlaff J, Altman DG (2009). Preferred reporting items for systematic reviews and meta-analyses: the prisma statement. *Journal of Clinical Epidemiology* **62**, 1006-12.

Morgan C, Abdul-Al R, Lappin JM, Jones P, Fearon P, Leese M, Croudace T, Morgan K, Dazzan P, Craig T, Leff J, Murray R (2006). Clinical and social determinants of duration of untreated psychosis in the AESOP first-episode psychosis study. *British Journal of Psychiatry* **189**, 446-52.

Morgan C, Lappin J, Heslin M, Donoghue K, Lomas B, Reininghaus U, Onyejiaka A, Croudace T, Jones PB, Murray RM, Fearon P, Doody GA, Dazzan P. (2014). Reappraising the long-term course and outcome of psychotic disorders: the aesop-10 study. *Psychological Medicine* **44**, 2713-26.

Munk-jorgensen P (1999). Has deinstitutionalization gone too far? Prologue. *European Archives of Psychiatry and Clinical Neuroscience* **249**, 113-4.

Opjordsmoen S, Friis S, Melle I, Haahr U, Johannessen JO, Larsen TK, Røssberg JI, Rund BR, Simonsen E, Vaglum P, McGlashan TH (2010). A 2-year follow-up of involuntary admission's influence upon adherence and outcome in first-episode psychosis. *Acta Psychiatrica Scandinavica* **121**, 371-6.

Patel V, Araya R, Chatterjee S, Chisholm D, Cohen A, De Silva M, Hosman C, McGuire H, Rojas G, van Ommeren M (2017). Treatment and prevention of mental disorders in low-income and middle-income countries. *Lancet* **370**, 991-1005.

Phan K, Xie A, Di Eusanio M, Yan TD (2014). A meta-analysis of minimally invasive versus conventional sternotomy for aortic valve replacement. *The Annals of Thoracic Surgery* **98**, 1499-511.

Pottick KJ, Mcalpine DD, Andelman RB (2000). Changing patterns of psychiatric inpatient care for children and adolescents in general hospitals, 1988-1995. *American Journal of Psychiatry* **157**, 1267-73.

Radua J, Ramella-Cravaro V, Ioannidis JP, Reichenberg A, Phiphopthatsanee N, Amir T, Yenn Thoo H, Oliver D, Davies C, Morgan C, McGuire P, Murray RM, Fusar-Poli P (2018). What causes psychosis? An umbrella review of risk and protective factors. *World psychiatry* **17**, 49-66.

Raftery J (1992). Mental health services in transition: the united states and the united kingdom. *British Journal of Psychiatry* **161**, 589-93.

Ropcke B, Eggers C (2005). Early-onset schizophrenia: a 15-year follow-up. European Child & Adolescent Psychiatry **14**, 341-50.

Salem MO, Moselhy HF, Attia H, Yousef S (2009). Psychogenic psychosis revisited: A follow up study. *International Journal of Health Sciences* **3**, 45-9.

Saxena S, Paraje G, Sharan P, Karam G, Sadana R (2006). The 10/90 divide in mental health research: trends over a 10-year period. *British Journal of Psychiatry* **188**, 81-2.

Saxena S, Sharan P, Garrido M, Saraceno B (2006). World health organization's mental health atlas 2005: implications for policy development. *World psychiatry* **5**, 179-84.

Schimmelmann BG, Huber CG, Lambert M, Cotton S, Mcgorry PD, Conus P (2008). Impact of duration of untreated psychosis on pre-treatment, baseline, and outcome characteristics in an epidemiological first-episode psychosis cohort. *Journal of Psychiatric Research* **42**, 982-90.

Schimmelmann BG, Huber CG, Lambert M, Cotton S, McGorry PD, Conus P (2008). Impact of duration of untreated psychosis on pre-treatment, baseline, and outcome characteristics in an epidemiological first-episode psychosis cohort. *Journal of Psychiatric Research* **42**, 982-90.

Schmidt M, Blanz B, Dippe A, Koppe T, Lay B (1995). Course of patients diagnosed as having schizophrenia during first episode occurring under age 18 years. *European Archives of Psychiatry and Clinical Neuroscience* **245**, 93-100.

Schoeler T, Petros N, Di Forti M, Klamerus E, Foglia E, Murray R, Bhattacharyya S (2017). Poor medication adherence and risk of relapse associated with continued cannabis use in patients with first-episode psychosis: a prospective analysis. *Lancet Psychiatry* **10**, 30233-x.

Sfetcu R, Musat S, Haaramo P, Ciutan M, Scintee G, Vladescu C, Wahlbeck K, Katschnig H. (2017). Overview of post-discharge predictors for psychiatric re-hospitalisations: a systematic review of the literature. *BMC Psychiatry* **24**, 017-1386.

Stirling J, White C, Lewis S, Hopkins R, Tantam D, Huddy A, Montague L (2003). Neurocognitive function and outcome in first-episode schizophrenia: a 10-year follow-up of an epidemiological cohort. *Schizophrenia Research* **65**, 75-86.

Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB (2000). Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of observational studies in epidemiology (MOOSE) group. JAMA **283**, 2008-12.

Sundermann O, Onwumere J, Kane F, Morgan C, Kuipers E (2014). Social networks and support in first-episode psychosis: exploring the role of loneliness and anxiety. *Social Psychiatry and Psychiatric Epidemiology* **49**, 359-66.

Tanskanen S, Moran N, Hinton M, Lloyd-Evans B, Crosby M, Killaspy H, Raine R, Pilling S, Johnson S (2011). Service user and carer experiences of seeking help for a first episode of psychosis: a UK qualitative study. *BMC Psychiatry* **11**, 11-157.

Tiihonen J, Mittendorfer-Rutz E, Majak M, Mehtälä J, Hoti F, Jedenius E, Enkusson D, Leval A, Sermon J, Tanskanen A, Taipale H. (2017). Real-world effectiveness of antipsychotic treatments in a nationwide cohort of 29823 patients with schizophrenia. *JAMA Psychiatry* **74**, 686-93.

Tohen M, Tsuang Mt, Goodwin DC (1992). Prediction of outcome in mania by mood-congruent or mood-incongruent psychotic features. *American Journal of Psychiatry* **149**, 1580-4.

Tohen M, Tsuang MT, Goodwin DC (1992). Prediction of outcome in mania by mood-congruent or mood-incongruent psychotic features. *American Journal of Psychiatry* **149**, 1580-1584

Tulloch AD, Fearon P, David AS. (2012). Timing, prevalence, determinants and outcomes of homelessness among patients admitted to acute psychiatric wards. *Social Psychiatry and Psychiatric Epidemiology* **47**(7), 1181-91.

Turner Ma, Boden Jm, Smith-Hamel C, Mulder RT (2009). Outcomes for 236 patients from a 2-year early intervention in psychosis service. *Acta Psychiatrica Scandinavica* **120**, 129-37.

Ucok A, Polat A, Cakir S, Genc A (2006). One year outcome in first episode schizophrenia. Predictors of relapse. *European Archives of Psychiatry and Clinical Neuroscience* **256**, 37-43.

Uggerby P, Nielsen RE, Correll CU, Nielsen J (2011). Characteristics and predictors of long-term institutionalization in patients with schizophrenia. *Schizophrenia Research* **131**, 120-6.

Van Os J, Linscott RJ, Myin-Germeys I, Delespaul P, Krabbendam I (2009). A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychological Medicine* **39**, 179-95.

Zipursky RB, Agid O (2015). Recovery, not progressive deterioration, should be the expectation in schizophrenia. *World Psychiatry* **14**, 94-6.

Figure Legends

Figure 1. The flowchart of the article selection process in the meta-analysis of hospitalisation and length of hospital stay during follow-up in patients with first episode psychosis (FEP).

Table 1. Meta-analysis of proportion of patients with first episode psychosis who were hospitalised at least once during a follow-up period

	Analysis	Meta-analysis					Heterogeneity			Publication bias
		n studies	Pooled prevalence (%)	95% CI		Between group p-value	I^2	Q-value	p-value	Trim and fill 95% CI [N studies trimmed]
Proportion of patients who were hospitalised at least once		58	55.4	50.3	60.5		98.5	3575.1	<0.001	Unchanged
Study year group						0.191				
	1966-1996	17	63.2	53.6	72.9		92.9	231.1	<0.001	Unchanged
	1997-2005	16	47.6	36.5	58.8		96.1	490.6	<0.001	Unchanged
	2006-2011	17	56.1	45.0	67.2		99.3	1743.7	<0.001	Unchanged
	2012-2017	8	46.6	30.7	62.5		98.2	564.4	<0.001	Unchanged
Study region						**0.013**				
	Asia	6	32.5	23.5	41.4		81.4	39.7	<0.001	Unchanged
	Australia and New Zealand	3	78.4	59.2	97.5		98.4	203.7	<0.001	Unchanged
	Europe	38	58.1	50.7	65.5		97.1	1212.1	<0.001	Unchanged
	North America	9	48.0	34.5	61.6		95.4	213.6	<0.001	Unchanged
	Middle East	1	64.0	63.1	64.9		0.0	0.0	1.000	N/A
	Multicentre	1	21.0	15.69	26.23		0.0	0.0	1.000	N/A
Assessment type						0.106				
	Case notes	18	62.5	52.1	72.9		99.2	1541.3	<0.001	Unchanged
	Interview	32	52.7	44.6	60.7		96.3	1047.5	<0.001	Unchanged
	Combination of both approaches	7	43.3	26.7	60.0		97.6	413.8	<0.001	Unchanged
Study settings						0.659				
	In-/out-patient psychiatric services	20	57.1	46.4	67.7		98.6	1557.4	<0.001	Unchanged
	Adult psychiatric hospitals	34	54.0	43.4	59.2		97.4	908.1	<0.001	Unchanged
	Community & early intervention services	4	45.0	22.1	67.8		98.9	420.3	<0.001	Unchanged
Length of follow-up categories						0.388				
	1-2 years	17	47.9	36.0	59.7		98.3	2155.2	<0.001	52.7 (40.3-65.0) [2]
	3-5 years	14	56.9	46.2	67.6		96.2	450.9	<0.001	Unchanged
	≥6 years	27	57.4	48.3	66.48		98.5	859.1	<0.001	Unchanged

Country socioeconomic status						**0.010**						
	High income	50	57.9	51.7	64.1			98.4	2833.6	<0.001		Unchanged
	Middle income	7	34.8	20.0	49.6			96.0	355.8	<0.001		42.9 (27.4-56.5) [2]
Baseline diagnoses						0.930						
	FEP	22	55.9	45.7	66.1			98.0	2351.3	<0.001		Unchanged
	FES	35	53.5	45.7	61.3			98.0	948.4	<0.001		Unchanged
	FEAP	1	54.2	34.2	74.1			0.0	0.0	1.000		NA

n, number; FEP, first episode psychosis; FU, follow up period; FEAP, first episode affective psychosis; N/A, not appropriate; CI, confidence intervals.

Table 2. Meta regression of moderators of proportion of patients with first episode psychosis who were hospitalised at least once during a follow-up

	Number of comparison	β	95% CI		p-value	R^2
Moderators						
Demographic factors						
Age (mean) at onset	15	0.060	-0.002	0.122	0.058	0.04
Age (mean) at first contact	41	-0.049	-0.092	-0.005	**0.028**	0.07
Males (%)	56	0.001	-0.004	0.006	0.762	0.00
White (%)	16	0.002	-0.002	0.005	0.344	0.00
Black (%)	16	0.004	0.000	0.009	0.075	0.13
Asian (%)	13	-0.002	-0.005	0.001	0.164	0.07
Clinical presentation and treatment						
Baseline psychotic symptoms(mean)	14	0.000	-0.005	0.005	0.935	0.00
Duration of untreated psychosis (days-mean)	12	0.000	-0.001	0.000	0.732	0.00
Duration of untreated psychosis (days-median)	8	-0.001	-0.003	0.001	0.202	0.09
Taking antipsychotic medications at baseline (%)	15	0.000	-0.003	0.004	0.934	0.00
Taking antipsychotic medications at follow up (%)	27	-0.002	-0.007	0.003	0.383	0.00
Compliance with antipsychotic medications during FU (%)	10	0.004	-0.002	0.010	0.185	0.08
Social factors						
Employed at baseline (%)	16	-0.002	-0.008	0.004	0.555	0.00
Single at baseline (%)	23	0.003	-0.002	0.008	0.203	0.03
Stable relationship at baseline	19	-0.011	-0.018	-0.004	**0.004**	0.33
Other factors						
Drop-out	54	-0.003	-0.007	0.000	0.080	0.04
Length of follow up	58	0.004	-0.006	0.013	0.488	0.00
Study year publication	58	-0.004	-0.010	0.002	0.161	0.02

DUP, duration of untreated psychosis; β, beta coefficient; CI, confidence intervals

Table 3. Meta-analysis of length of inpatient stays during a follow-up in patients with first episode psychosis

	Analysis	Meta-analysis					Heterogeneity				Publication bias
		n studies	Pooled mean	95% CI		Between group p-value	I^2	Q-value	p-value		Trim and fill 95% CI [N studies trimmed]
Average length of inpatient stay during a follow-up		26	116.7	95.1	138.3		99.5	4435.1	<0.001		Unchanged
Study year group						**0.058**					
	1966-1995	5	192.3	129.7	254.8		89.2	37.1	<0.001		216.8 (126.3-307.3) [1]
	1996-2002	5	129.9	78.8	180.9		98.9	368.1	<0.001		Unchanged
	2003-2009	7	97.7	55.3	139.9		99.8	3041.4	<0.001		126.0 (54.0-197.0) [1]
	2010-2017	7	96.6	54.0	139.2		99.3	852.8	<0.001		94.6 (67.2-121.9) [1]
Study region						0.326					
	Asia	4	71.1	-25.6	167.7		99.0	349.4	<0.001		60.2 (28.8-91.7) [1]
	Australia and New Zealand	1	25.9	-167.2	219.0		0.0	0.0	1.000		N/A
	Europe	18	145.7	99.2	192.2		99.6	2416.1	<0.001		Unchanged
	North America	3	175.0	47.5	302.5		99.8	51.6	<0.001		Unchanged
Assessment type						0.798					
	Case notes	3	114.2	54.9	173.5		98.0	101.3	<0.001		Unchanged
	Interview	20	119.3	95.0	143.5		99.5	3967.9	<0.001		Unchanged
	Combination of both approaches	1	83.1	-20.7	186.9		0.0	0.0	1.000		N/A
Study settings						0.794					
	In-/out-patient psychiatric services	11	114.9	81.1	148.6		99.7	3573.1	<0.001		Unchanged
	Adult psychiatric hospitals	11	128.6	92.1	165.2		98.3	596.3	<0.001		Unchanged
	Community & early intervention services	1	92.8	-18.2	203.8		0.0	0.0	1.000		N/A
Country socioeconomic status						0.178					
	High income	23	120.5	97.7	143.3		99.5	4433.8	<0.001		Unchanged
	Middle income	1	47.8	-55.6	151.2		0.0	0.0	1.000		N/A
Baseline diagnoses						0.345					
	FEP	8	103.8	33.8	173.8		99.8	658.4	<0.001		Unchanged
	FES	15	159.5	106.2	212.7		99.8	2164.0	<0.001		Unchanged
	FEAP	2	81.8	-58.4	222.0		96.3	27.3	<0.001		N/A

n, number; FEP, first episode psychosis; FU, follow up period; FEAP, first episode affective psychosis; N/A, not appropriate; CI, confidence intervals

Table 4. Meta-regression of moderators of an average length of inpatient stay during a follow-up during a follow up in patients with first episode psychosis

	Number of comparison	β	95% CI		p-value	R^2
Moderators						
Demographic factors						
Age (mean) at onset	11	3.604	-1.039	8.246	0.128	0.00
Age (mean) at first contact	15	5.150	-1.212	11.512	0.113	0.00
Males (%)	20	-0.566	-3.049	1.916	0.655	0.00
White (%)	8	-0.181	-0.219	-0.143	**0.000**	0.12
Black (%)	5	2.905	1.273	4.537	**0.000**	0.14
Asian (%)	4	0.072	-0.507	0.651	0.808	0.00
Clinical presentation and treatment						
Baseline psychotic symptoms(mean)	10	-0.019	-0.036	-0.003	**0.018**	0.08
Duration of untreated psychosis (days-mean)	9	-0.005	-0.158	0.149	0.953	0.00
Duration of untreated psychosis (days-median)	4	0.303	0.266	0.340	**0.000**	0.11
Taking antipsychotic medications at baseline (%)	4	1.289	-0.804	3.383	0.227	0.00
Taking antipsychotic medications at follow up (%)	8	1.249	-1.756	4.254	0.415	0.00
Compliance with antipsychotic medications during FU (%)	3	1.910	-1.281	5.177	0.237	0.17
Social factors						
Employed at baseline (%)	5	2.137	-1.010	5.284	0.183	0.00
Single at baseline (%)	7	-1.747	-4.776	1.282	0.258	0.01
Stable relationship at baseline	5	5.930	-4.082	15.942	0.246	0.00
Other factors						
Drop-out	22	1.091	0.033	2.149	0.043	0.10
Length of follow up	22	11.707	6.577	16.838	**0.000**	0.21
Study year publication	22	-4.413	-7.456	-1.370	**0.004**	0.15

DUP, duration of untreated psychosis; β, beta coefficient; CI, confidence intervals